

CLAIMS

We claim:

5 1. A method of treating neurodegeneration in a patient,  
comprising

10 identifying a patient at risk for neurodegeneration; and  
administering to the patient a therapeutically effective  
amount of SUMOylation blocker.

15 2. The method of claim 1, wherein the SUMOylation blocker is  
an inhibitor E1 SUMO activating enzyme.

3. The method of claim 1, wherein the SUMOylation blocker is  
an inhibitor E2 SUMO conjugating enzyme.

20 4. The method of claim 1, wherein the SUMOylation blocker is  
an inhibitor E3 SUMO ligating enzyme.

25 5. The method of claim 4, wherein the inhibitor of E3 SUMO  
ligating enzyme is a PIAS protein.

6. A method of treating neurodegeneration in a patient,  
comprising

30 identifying a patient at risk for neurodegeneration; and  
administering to the patient a therapeutically effective  
amount of deSUMOylation enhancer.

35 7. The method of claim 6, wherein the deSUMOylation enhancer  
is SUMO isopeptidase.

8. A method of treating neurodegeneration in a patient,

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comprising

identifying a patient at risk for neurodegeneration; and  
5 administering to the patient a therapeutically effective  
amount of a Ubiquitination activator.

9. The method of claim 8, wherein the Ubiquitination  
10 activator is an activator of E1 Ubiquitin activating enzyme.

10. The method of claim 8, wherein the Ubiquitination  
activator is an activator of E1 Ubiquitin conjugating enzyme.

15 11. The method of claim 8, wherein the Ubiquitination  
activator is an activator of E3 Ubiquitin ligating enzyme.

12. A method of treating neurodegeneration in a patient,  
20 comprising

identifying a patient at risk for neurodegeneration; and  
administering to the patient a therapeutically effective  
amount of deUbiquitination inhibitor.

25 13. The method of claim 12, wherein the deUbiquitination  
inhibitor is an inhibitor of Ubiquitin isopeptidase.

14. A method of treating polyglutamine-expansion-related  
30 neurodegeneration in a patient, comprising

identifying a patient at risk for polyglutamine-  
expansion-related neurodegeneration; and  
administering to the patient a therapeutically effective  
35 amount of SUMOylation blocker.

15. The method of claim 14, wherein the SUMOylation blocker

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is an inhibitor E1 SUMO activating enzyme.

5 16. The method of claim 14, wherein the SUMOylation blocker  
is an inhibitor E2 SUMO conjugating enzyme.

10 17. The method of claim 14, wherein the SUMOylation blocker  
is an inhibitor E3 SUMO ligating enzyme.

18. The method of claim 17, wherein the inhibitor of E3 SUMO  
ligating enzyme is a PIAS protein.

15 19. A method of treating polyglutamine-expansion-related  
neurodegeneration in a patient, comprising  
identifying a patient at risk for polyglutamine-  
expansion-related neurodegeneration; and  
20 administering to the patient a therapeutically effective  
amount of deSUMOylation enhancer.

25 20. The method of claim 19, wherein the deSUMOylation  
enhancer is SUMO isopeptidase.

21. A method of treating polyglutamine-expansion-related  
neurodegeneration in a patient, comprising  
identifying a patient at risk for polyglutamine-  
30 expansion-related neurodegeneration; and  
administering to the patient a therapeutically effective  
amount of a Ubiquitination activator.

35 22. The method of claim 21, wherein the Ubiquitination  
activator is an activator of E1 Ubiquitin activating enzyme.

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23. The method of claim 21, wherein the Ubiquitination  
activator is an activator of E2 Ubiquitin conjugating enzyme.

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24. The method of claim 21, wherein the Ubiquitination  
activator is an activator of E3 Ubiquitin ligating enzyme.

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25. A method of treating polyglutamine-expansion-related  
neurodegeneration in a patient, comprising

identifying a patient at risk for polyglutamine-  
expansion-related neurodegeneration; and

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administering to the patient a therapeutically effective  
amount of deUbiquitination inhibitor.

26. The method of claim 25, wherein the deUbiquitination  
inhibitor is an inhibitor of Ubiquitin isopeptidase.

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27. A method of treating a neurodegenerative disease in a  
patient, comprising administering to the patient a  
therapeutically effective amount of SUMOylation blocker.

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28. The method of claim 27, wherein the SUMOylation blocker  
is an inhibitor E1 SUMO activating enzyme.

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29. The method of claim 27, wherein the SUMOylation blocker  
is an inhibitor E2 SUMO conjugating enzyme.

30. The method of claim 27, wherein the SUMOylation blocker  
is an inhibitor E3 SUMO ligating enzyme.

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31. The method of claim 30, wherein the inhibitor of E3 SUMO  
ligating enzyme is a PIAS protein.

32. The method of claim 27, wherein the neurodegenerative disease is one of more of the group consisting of Huntington's disease, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, Kennedy's disease, SCA1, DRPLA, epilepsy, diabetes mellitus, spongiform encephalopathy, prion-related disease, Machado-Joseph's disease and schizophrenia.

33. A method of treating a neurodegenerative disease in a patient, comprising administering to the patient a therapeutically effective amount of deSUMOylation enhancer.

34. The method of claim 33, wherein the deSUMOylation enhancer is SUMO isopeptidase.

35. The method of claim 33, wherein the neurodegenerative disease is one of more of the group consisting of Huntington's disease, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, Kennedy's disease, SCA1, DRPLA, epilepsy, diabetes mellitus, spongiform encephalopathy, prion-related disease, Machado-Joseph's disease and schizophrenia.

36. A method of treating a neurodegenerative disease in a patient, comprising administering to the patient a therapeutically effective amount of a Ubiquitination activator.

37. The method of claim 36, wherein the Ubiquitination activator is an activator of E1 Ubiquitin activating enzyme.

38. The method of claim 36, wherein the Ubiquitination activator is an activator of E1 Ubiquitin conjugating enzyme.

39. The method of claim 36, wherein the Ubiquitination  
5 activator is an activator of E3 Ubiquitin ligating enzyme.

40. A method of treating a neurodegenerative disease in a  
patient, comprising administering to the patient a  
10 therapeutically effective amount of a deUbiquitination  
inhibitor.

41. The method of claim 40, wherein the deUbiquitination  
15 inhibitor is an inhibitor of Ubiquitin isopeptidase.

42. The method of claim 40, wherein the neurodegenerative  
disease is one of more of the group consisting of Huntington's  
disease, Alzheimer's disease, Parkinson's disease, amyotrophic  
20 lateral sclerosis, Kennedy's disease, SCA1, DRPLA, epilepsy,  
diabetes mellitus, spongiform encephalopathy, prion-related  
disease, Machado-Joseph's disease and schizophrenia.

43. A method of treating Huntington's disease in a patient,  
25 comprising administering to the patient a therapeutically  
effective amount of a SUMOylation blocker.

44. A method of treating Huntington's disease in a patient,  
30 comprising administering to the patient a therapeutically  
effective amount of a deSUMOylation enhancer.

45. A method of treating Huntington's disease in a patient,  
35 comprising administering to the patient a therapeutically  
effective amount of a Ubiquitination activator.

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46. A method of treating Huntington's disease in a patient,  
comprising administering to the patient a therapeutically  
5 effective amount of a deUbiquitination inhibitor.

47. A method of treating Kennedy's disease in a patient,  
comprising administering to the patient a therapeutically  
10 effective amount of a SUMOylation blocker.

48. A method of treating Kennedy's disease in a patient,  
comprising administering to the patient a therapeutically  
15 effective amount of a deSUMOylation enhancer.

49. A method of treating Kennedy's disease in a patient,  
comprising administering to the patient a therapeutically  
20 effective amount of a Ubiquitination activator.

50. A method of treating Kennedy's disease in a patient,  
comprising administering to the patient a therapeutically  
25 effective amount of a deUbiquitination inhibitor.

51. A method of treating spinocerebellar ataxia in a patient,  
comprising administering to the patient a therapeutically  
30 effective amount of a SUMOylation blocker.

52. A method of treating spinocerebellar ataxia in a patient,  
comprising administering to the patient a therapeutically  
35 effective amount of a deSUMOylation enhancer.

53. A method of treating spinocerebellar ataxia in a patient,  
comprising administering to the patient a therapeutically  
effective amount of a Ubiquitination activator.

54. A method of treating spinocerebellar ataxia in a patient,  
5 comprising administering to the patient a therapeutically  
effective amount of a deUbiquitination inhibitor.

55. A method of treating dentatorubral-pallidoluysian atrophy  
10 in a patient, comprising administering to the patient a  
therapeutically effective amount of a SUMOylation blocker.

56. A method of treating dentatorubral-pallidoluysian atrophy  
15 in a patient, comprising administering to the patient a  
therapeutically effective amount of a deSUMOylation enhancer.

57. A method of treating dentatorubral-pallidoluysian atrophy  
in a patient, comprising administering to the patient a  
20 therapeutically effective amount of a Ubiquitination  
activator.

58. A method of treating dentatorubral-pallidoluysian atrophy  
25 in a patient, comprising administering to the patient a  
therapeutically effective amount of a deUbiquitination  
inhibitor.

59. A method of treating protein-aggregation-related  
30 neurodegeneration in a patient, comprising administering to  
the patient a therapeutically effective amount of a  
SUMOylation blocker.

60. A method of treating protein-aggregation-related  
35 neurodegeneration in a patient, comprising administering to  
the patient a therapeutically effective amount of a

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deSUMOylation enhancer.

5 61. A method of treating protein-aggregation-related neurodegeneration in a patient, comprising administering to the patient a therapeutically effective amount of a Ubiquitination activator.

10 62. A method of treating protein-aggregation-related neurodegeneration in a patient, comprising administering to the patient a therapeutically effective amount of a deUbiquitination inhibitor.

15 63. A method of treating Machado-Joseph's disease in a patient, comprising administering to the patient a therapeutically effective amount of a SUMOylation blocker.

20 64. A method of treating Machado-Joseph's disease in a patient, comprising administering to the patient a therapeutically effective amount of a deSUMOylation enhancer.

25 65. A method of treating Machado-Joseph's disease in a patient, comprising administering to the patient a therapeutically effective amount of a Ubiquitination activator.

30 66. A method of treating Machado-Joseph's disease in a patient, comprising administering to the patient a therapeutically effective amount of a deUbiquitination inhibitor.

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